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I-ELCAP Moves From Weill Cornell To Arizona State; PIs Move To Mount Sinai

By Paul Goldberg

A controversial program aimed at screening current and former smokers for signs of early-stage lung cancer is in the process of departing from Weill Cornell Medical College.

The research group, called the International Early Lung Cancer Action Program, said it has moved its "coordinating site" to the Arizona State University's Biodesign Institute in Tempe, and top academic leaders of the group now appear on the web site of Mount Sinai School of Medicine.

I-ELCAP, led by radiologist Claudia Henschke, has been plagued with problems, which included revelations of undisclosed conflicts of interest, receiving funding from a tobacco company, and retractions of key scientific claims about effectiveness of screening for early lung cancer.

"I can confirm that Dr. Henschke and her team are indeed transitioning

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In the Cancer Centers:

Ratain To Lead New Center For Personalized Therapeutics At University of Chicago

UNIVERSITY OF CHICAGO and its Medical Center approved the creation of the University of Chicago Center for Personalized Therapeutics under the direction of **Mark Ratain**, the Leon O. Jacobson Professor of Medicine and chairman of the Committee on Clinical Pharmacology and Pharmacogenomics at the University of Chicago and the chair of the Pharmacogenetics of Anticancer Agents Research Group.

The center will bring together faculty from the basic and clinical sciences to focus on issues raised by progress in the understanding of human genetics, including the relationships between genetic variation, disease and drug metabolism; and the emerging field of personalized medicine. It will involve researchers working in pharmacology, genetics, informatics and clinical care, as well as medical education and public policy.

The center will eventually establish an outpatient clinic and an inpatient consultation service. The center will develop systems for efficient collection, storage and clinical application of genetic data and train physicians in the use of personalized genetic information as a tool in patient care. It will focus initially on genotyping about 1,000 patients, including those from diverse outpatient clinics (including but not limited to cancer).

As more information on the clinical significance of genetic variations

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Controversial Lung Screening Program Leaves Weill Cornell

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to Mount Sinai in the near future," said John Rodgers, a spokesman for New York-Presbyterian Hospital/Weill Cornell Medical Center. "I don't have any more details than that or a firm date."

A spokesman for the Arizona institution confirmed the move. "Claudia Henschke and [collaborator] David Yankelevitz were appointed adjunct faculty at Arizona State University in late 2009," said Joe Caspermeyer, a spokesman. "ASU's Biodesign Institute has become the coordinating site to provide administrative management of the International Early Detection of Lung Cancer Action Program."

Caspermeyer said a formal announcement regarding the affiliation with will be made at I-ELCAP conference March 19-21. Since the Biodesign Institute is not a clinical facility and its patent institution doesn't have a medical school, it's unclear how I-ELCAP would go about providing protection for patients involved in its experiments.

A spokesman from Mount Sinai, where the website now lists Henschke and Yankelevitz as adjunct faculty, didn't respond to questions from The Cancer Letter by deadline.

I-ELCAP's departure ends a two-decade-long relationship between the research group and the institution where it was started in 1991. Weill Cornell helped the screening group obtain substantial funding from New York's settlement with tobacco companies, and it obtained and licensed patents for screening technology developed by Henschke, Yankelevitz, and their collaborators (The Cancer Letter. Jan. 18, 2008).

Ten years ago, top Weill Cornell officials acted as fiduciaries in a Henschke-run non-profit organization that received a $3.6 million from the parent company of cigarette maker Liggett Group Ltd. (The Cancer Letter, March 28, 2008). After reports of undeclared conflicts of interest and tobacco funding appeared in this publication and on the front page of The New York Times, Weill Cornell officials steadfastly defended receiving and disbursing Liggett money.

I-ELCAP's relationships with industry were controversial, as some of the group's intellectual property was licensed by General Electric, a company that manufactures CT scanners. News stories prompted the key journals that published I-ELCAP papers to correct the record, noting undisclosed conflicts on the part of I-ELCAP investigators. Corrections appeared in The New England Journal of Medicine, the Journal of the American Medical Association, The Lancet, Nature Clinical Practice Oncology, Cancer, and The Oncologist.

NEJM, which published I-ELCAP's highest-profile paper in its Oct. 26, 2006, issue, was officially sanctioned by the Accreditation Council for Continuing Medical Education for offering CME credit in conjunction with that paper while knowing about conflicts of interest on the part of researchers and choosing not to require disclosure (The Cancer Letter, Jan. 9, 2009).

Centers Moved Away From I-ELCAP Screening

Henschke and her supporters argue that the findings from their single-arm demonstration project show that their regimen of screening can make lung cancer into a curable disease. However, no major professional group has endorsed changing the standard of care to include regular screening of former and current smokers.

NCI is conducting a randomized trial designed to compare CT screening with standard chest x-ray in their impact on mortality.

Screening based on the I-ELCAP protocol is now available primarily in small and mid-sized hospitals, and the list of major centers that once offered I-ELCAP screening but are no longer enrolling new patients seems to be growing.

According to I-ELCAP's website, Weill Cornell has become the latest major center to stop enrolling new patients for screening.

However, it appears that appointments can still

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be made by leaving a message on a Weill Cornell telephone number listed in the I-ELCAP website alongside Henschke's name. "As we are understaffed, it may take one or two days for us to return your call, but we will call you as soon as possible," the outgoing message states.

If Mount Sinai decides to provide a home for I-ELCAP, it would be breaking ranks with other major academic institutions, which were initially involved in the I-ELCAP screening program, but have since stopped accepting patients.

I-ELCAP's website includes a list of member sites which continues to list institutions that are no longer enrolling new participants. These include: City of Hope National Medical Center, H. Lee Moffitt Cancer Center, Karmanos Cancer Institute, Columbia University Medical Center, Weill Cornell, Memorial Sloan-Kettering Cancer Center, Roswell Park Cancer Institute, and State University of New York.

In New York state alone, 16 institutions are listed as I-ELCAP member sites. However, all but two of them are currently not enrolling new participants.

Mount Sinai appears on the I-ELCAP list, with Henschke identified as the principal investigator. However, the list doesn't indicate whether patients are being screened at that institution.

Audit Called For But Never Conducted

The controversy over I-ELCAP's work is not limited to conflicts of interest and tobacco money.

The American Cancer Society, which funded a part of I-ELCAP's work, has called for an audit of the group's data. "I am very concerned about the I-ELCAP data and the I-ELCAP findings" Otis Brawley, the society's chief medical officer, said at a meeting convened to review a proposal to include I-ELCAP data in a pooled analysis of lung screening trials. "I think we can only use the I-ELCAP data if there is an external audit to verify that data, and there is an independent reanalysis of the data" (The Cancer Letter, Sept. 26, 2008).

At the time, Bruce Chabner, clinical director of the Massachusetts General Hospital MGH Cancer Center, similarly called for an audit of the I-ELCAP data.

"The results of this key lung cancer prevention trial, heralded as evidence for the value of CT screening for lung cancer, have become increasingly ambiguous, a situation that can only be dispelled by auditing the trial," Chabner wrote in the September 2008 issue of The Oncologist, a journal he edits.

Dispute over I-ELCAP's conclusions was summarized in the Sept. 26, 2008, issue of The Cancer Letter.

This discussion is reprinted below:

Chabner's call for an audit was triggered by new information that turned up in an exchange of letters between Henschke and Peter Bach, a pulmonologist and health systems researcher at Memorial Sloan-Kettering Cancer Center.

Bach challenged the I-ELCAP claims about the deaths of patients who had declined treatment after being told that they had stage I disease. The I-ELCAP paper published in the Oct. 26, 2006, issue of NEJM claimed that eight patients who were told that they had stage I disease but declined further care had died.

This cohort is important to Henschke's argument for screening, because it would help establish that patients diagnosed through CT have clinically relevant disease. Though the original NEJM paper didn't specify the cause of death, in a subsequent exchange of letters, Henschke noted that the eight patients had died of lung cancer.

Later, in the January 2008 issue of The Oncologist, Henschke claimed that the number of such deaths had gone from eight to 13, and supplied the follow-up times for these untreated subjects.

However, in recent months, the I-ELCAP claim that patients who declined care faced certain death started to erode. In a letter published in the July 30 issue of NEJM, Henschke acknowledged that five of the eight untreated subjects in her original paper had been misclassified and had advanced disease at the time of diagnosis.

Though Henschke's admission to NEJM struck at the heart of her original paper, it was published as a letter to the editor. Also, nothing was said about the author's reasons for correcting the record.

"We find it interesting that this 'correction' was published as a letter to NEJM, rather than a formal correction or retraction," Chabner wrote in his editorial in [September, 2008 issue of] The Oncologist. "Given the importance of this recent revelation, either would have seemed more appropriate."

Challenged to respond to Bach's letter, Henschke acknowledged that misclassification of untreated subjects was more widespread than she noted in the NEJM letter less than two months earlier. "I have addressed [Bach's] particular concern regarding classification of the untreated stage I cases of lung cancer recently and acknowledge the same reclassification issue with the five additional cases of this kind reported in The Oncologist," Henschke wrote to The Oncologist.

Henschke's response doesn't address the deeper

concerns raised by Bach.

Bach argues that the additional five patients would have had to be placed on the study and die over 15 months between the publication dates of the NEJM paper (October 2006) and the publication date of The Oncologist paper (January 2008).

"This means that all five of the additional subjects had to both enter the study and die from lung cancer during the time that passed between the papers," Bach wrote to The Oncologist. "For this to occur, the time interval between the two publications had to be as long as the minimum follow-up time needed for all five subjects to both enter the study and die. But not that much time actually passed."

According to Henschke's data, the survival time for one of the subjects was 20 months, five months longer than the interval between the two publications.

Also, Bach noted that there appear to be no signs of censoring in the untreated group. In a study with a rolling entry, censoring is used to black out patients whenever follow-up data are incomplete at the time of analysis.

Bach writes that the probability that none of the 13 patients were censored was low. "It is 1.6 percent (the product of the individual 13 probabilities of not being censored," he wrote. "Not impossible, but highly improbable.

"Put together, I worry that the data… may be biased in a manner that reduces the survival estimate for untreated subjects," he wrote. "If, for example, IELCAP investigators were only capturing information on untreated subjects after they died, this would explain why all the subjects in the graph died, and none were censored.

"But the problem with this approach is that study inclusion is associated with study outcome, and in this case the bias would ensure that the death rate is always 100 percent (because no new subjects are added until they die.)."

In the Cancer Centers:

City of Hope Wins Nearly $17M For Islet And Stem Cell Centers

(Continued from page 1)

is acquired, the team will expand this genetic profile for each patient.

CITY OF HOPE Department of Information Sciences received a $16.9 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases for a distributing center for human islet cells and to create a similar center for intestinal stem cell research. Part of the funding—a five-year, $14 million contract—will advance the department's position as the nation's islet cell distribution coordination center, and the remaining $2.9 million grant will fund the creation of a similar center for the NIDDK's recently formed Intestinal Stem Cell Consortium. City of Hope established the Islet Distribution Coordinating Center in 2002 to facilitate the distribution of islets produced by 14 islet isolation facilities across the U.S. Joyce Niland, the Edward and Estelle Alexander Chair in Information Sciences and chair of the Department of Information Sciences, is principal investigator for the contract and the grant.

In another award, the National Heart, Lung, and Blood Institute awarded City of Hope an $8.6 million contract to facilitate stem cell research. The five-year contract is the first from the NHLBI to focus on development and manufacturing of stem cell therapies. City of Hope will manufacture the therapies in its Center for Biomedicine & Genetics.

Also, epidemiologist Susan Neuhausen joined City of Hope as professor of population sciences and the first Morris & Horowitz Families Professor in Cancer Etiology and Outcomes Research. Neuhausen joined City of Hope from the University of California, Irvine, where she served as associate director of the Genetic Epidemiology Research Institute and professor in the departments of epidemiology and pediatrics. At UCI, she performed research primarily on breast and prostate cancers and celiac disease. Neuhausen also holds a patent for her discovery of a specific chromosome mutation linked to prostate cancer risk.

ROSWELL PARK CANCER INSTITUTE received a grant for $1.7M from the National Institute for Allergies and Infectious Disease to study human therapeutics targeting acute radiation syndrome. **Andrei Gudkov**, senior vice president, basic science, and chairman of Cell Stress Biology, is the principal investigator.

ROBERT H. LURIE COMPREHENSIVE CANCER CENTER of Northwestern University member **Melina Kibbe** was honored at the White House on Jan. 13 as a recipient of the Presidential Early Career Award for Scientists and Engineers. This is the highest honor given by the U.S. government to outstanding scientists and engineers who are in the

early stages of their independent research careers. Kibbe, associate professor of surgery at Northwestern University's Feinberg School of Medicine, is a vascular surgeon at Northwestern Memorial Hospital and co-chief of the vascular surgery service and director of the Vascular Laboratory at the Jesse Brown VA Medical Center. Kibbe, who was nominated for the award by the U.S. Department of Veterans Affairs, will receive funding from the department for five years as part of this award.

MEMORIAL SLOAN-KETTERING CANCER CENTER said **Shanu Modi**, a physician on the Breast Cancer Medicine Service, has been named the incumbent of the Patricia and James Cayne Chair for Junior Faculty. Modi, a medical oncologist, is involved in phase I and phase II trials to evaluate novel anti-HER2 therapies. Modi came to MSKCC in 2001 as a breast cancer research fellow and joined the faculty in 2005.

Breast Cancer:

Report Calls For Better Risk Stratification And A New Name For Ductal Carcinoma In Situ

An article and commentary published online Jan. 13 in the Journal of the National Cancer Institute review available data on diagnosis and management of ductal carcinoma in situ, and offer recommendations for the field.

These include identification of better risk stratification methods, consideration of the elimination of the word "carcinoma" from the name, and further investigation into whether imaging technology and guidelines can be modified to focus on high-risk lesions.

The commentary is the conference statement from the NIH state-of-the-science conference on DCIS. At the conference last September, speakers and panel members focused on five questions that tackled incidence, risk factors, screening, prognostic factors, and treatment of DCIS. The commentary provides a summary of the answers to those questions based on available research data, input from conference participants, and the panel's assessment.

"Clearly, the diagnosis and management of DCIS is highly complex with many unanswered questions, including the fundamental natural history of untreated disease," the panel writes. "Thus, the primary question for future research must focus on the accurate identification of patient subsets diagnosed with DCIS."

The article by Beth Virnig, of the Division of Health Policy and Management, University of Minnesota School of Public Health, and colleagues is a review of literature on DCIS research from 1965 through January 2009. The review was generated for the conference to serve as a background paper.

Virnig covers the five questions discussed at the conference but also highlights areas that need further investigation: associations between mammography use and DCIS incidence and the modification of imaging and treatment guidelines to focus on clinically relevant tumors.

Efforts should also be made to make full use of biomarkers, such as HER2 status and necrosis, to determine risk status, according to the paper. "This would allow for focusing aggressive treatment on those who have the greatest probability of benefit," the authors write.

The commentary is available at http://www.oxfordjournals.org/our_journals/jnci/press_releases/allegra.final.djp485.pdf. The article is available at: http://www.oxfordjournals.org/our_journals/jnci/press_releases/virnig.final.djp482.pdf.

Tobacco Control:

ACS Report Lists Challenges For Global Tobacco Control

A new American Cancer Society report outlines 21 challenges and needs for global tobacco control, covering the wide range of issues to be addressed and expertise needed to reduce the rising tide of tobacco use worldwide, particularly in the low- and middle-income nations that are the target of the multinational tobacco industry.

The report is published early online and will appear in the January/February issue of CA: A Cancer Journal for Clinicians.

The report's authors, led by Thomas Glynn, director of Cancer Science and Trends for ACS, point out that the globalization of tobacco began with the European exploration of the New World more than 500 years ago. But it is only in the past 50 years that public health has responded to the death, disease, and economic disruption caused by tobacco use.

Tobacco now has at least 1.3 billion users and kills more than 14,500 people every day, while debilitating and sickening many times that number. The report lists activities, policies, and interventions that must be increased or in some cases decreased in order to be successful in reducing the rising tide of tobacco use.

The report calls for the following:

—Increase support for and adherence to the Framework Convention on Tobacco Control: The report calls this the single most important action in the effort to eliminate tobacco-related death and disease, saying all governments should be encouraged to join the more than 165 nations who already have ratified the treaty, and that those who have joined the Framework should faithfully implement it.

—Increase tobacco taxes: Raising tobacco taxes is considered perhaps the most effective intervention to reduce tobacco use.

—Increase access to comprehensive treatment for tobacco dependence: With more than 1.3 billion tobacco users in the world today, if only half of them wished to stop their tobacco use, there would be need for access to tobacco dependence treatment for greater than 650 million tobacco users. Furthermore, the World Bank has estimated that more than 180 million lives could be saved in just the first half of this century if the prevalence of current tobacco users were cut in half by 2020, and providing access to adequate treatment would be a cornerstone of that approach.

—Increase media-based tobacco counter-marketing campaigns: Although the tobacco industry will always far outspend tobacco control advocates, novel, entertaining, cutting-edge tobacco counter-marketing campaigns have been shown to attract attention and support far beyond the amount of funds spent and to have a direct effect on reducing tobacco use.

—Increase regulation of all tobacco products: Tobacco is the most unregulated consumer product on the market today, exempt from important basic consumer protections, such as ingredient disclosure, product testing, accurate labeling, and restrictions on marketing to children.

—Increase health warnings on tobacco packaging: As warnings become more graphic, tobacco users are more likely to pay attention to them.

—Increase availability of tobacco health/economic information to the general public: Many tobacco users, policymakers, and even health care professionals are largely unaware, or only vaguely aware, of the other cancers, heart disease, lung disease, pre– and postnatal conditions, etc that are caused by tobacco use.

—Increase primacy of health over commerce in trade agreements: Successful arguments have been made that excluding tobacco from trade agreements is compatible with international law, which provides for other harmful products such as landmines to be exempted. In addition, the World Trade Organization has declared that human health is an important consideration and that if necessary, governments may "put aside WTO commitments" to protect human life.

—Increase basic biomedical and applied tobacco control research

—Increase the extent and accuracy of tobacco epidemiologic and surveillance data

—Increase litigation aimed at the tobacco industry

—Decrease tobacco use by physicians and other health care providers: Many physicians and health care providers continue to use tobacco, with use reported to be as high as 50% or more in some countries

—Decrease targeting of women: The WHO has estimated that the prevalence of smoking among women worldwide will be 20% by 2025, compared with the 12% of the world's women who currently smoke.

—Decrease exposure to secondhand smoke: Providing smoke-free environments has been proven to not only protect nonsmokers, but also encourage smokers to quit and focus greater attention on the need for tobacco control measures.

—Decrease illicit trade and smuggling

—Decrease duty-free and reduced–cost sales of tobacco

—Decrease tobacco advertising, promotion, and sponsorship

—Decrease misleading tobacco product claims/ descriptors

—Decrease targeting of youth

—Decrease subsidies for tobacco production

—Decrease youth access to tobacco

The report says there are many other challenges not discussed in the report and that, while "resources… will never be enough to address all of these challenges," actions taken with the resources currently available will have a significant effect on global health. Finally, the report points to an issue it says rises above all others when considering the potential to reverse the global tobacco epidemic: the need for skilled, dedicated people to address the issues outlined in the report.

FDA News:

FDA Unveils First Phase Of Transparency Initiative

FDA released the first phase of its "Transparency Initiative," which is designed to explain agency operations, how it makes decisions, and the drug approval process.

The agency has posted a Web-based curriculum

called "FDA Basics," aimed at helping the public better understand what the agency does. The curriculum is accessible via a link on the FDA Web site: http://www.fda.gov/AboutFDA/Basics.

In one of her first acts after assuming the office last spring, FDA Commissioner Margaret Hamburg announced the formation of an internal task force to develop recommendations for enhancing the transparency of the FDA's operations and decision-making processes.

The Transparency Initiative was launched in response to the Obama Administration's commitment to openness in government. "This initiative will make information about the FDA more user-friendly and accessible to the public," Hamburg said. "It fosters a better understanding about what we do."

In recent months, the Transparency Task Force solicited public input on improving agency transparency through a public docket, an online blog, and two public meetings. The Task Force received hundreds of comments from regulated industry, consumers, patients, health care providers, and others. As a result of comments from the public, the Task Force decided to develop its recommendations in three phases. FDA Basics represents the result of the initial phase, to be followed by two additional phases.

In phase two of the initiative, the Task Force intends to make recommendations regarding how to make information about agency activities more transparent, useful, and understandable to the public, in a manner compatible with the agency's goal of protecting confidential information, as appropriate.

In the final phase of the initiative, the Task Force intends to make recommendations regarding FDA's transparency to regulated industries. For more information: http://www.fda.gov/transparency.

NCI News:

TCGA Identifies Subtypes Of Glioblastoma Multiforme

The most common form of malignant brain cancer in adults, glioblastoma multiforme (GBM), is not a single disease but appears to be four distinct molecular subtypes, according to a study by the Cancer Genome Atlas (TCGA) Research Network.

The researchers of this study also found that response to aggressive chemotherapy and radiation differed by subtype. Patients with one subtype treated with this strategy appeared to succumb to their disease at a rate approximately 50 percent slower than patients treated with less aggressive therapy. This effect was seen to a lesser degree in two of the subtypes and not at all in the fourth subtype.

Although the findings do not affect current clinical practice, the researchers said the results may lead to more personalized approaches to treating groups of GBM patients based on their genomic alterations.

The study, published Jan. 19 in Cancer Cell, provides a solid framework for investigation of targeted therapies that may improve the near uniformly fatal prognosis of this cancer. The research team for TCGA is a collaborative effort funded by the NCI and the National Human Genome Research Institute.

"TCGA is mobilizing the entire cancer community to find new strategies in detecting and treating cancer faster," said NIH Director Francis Collins. "These findings are just a hint of what we expect to result from the comprehensive data generated by TCGA over the next few years."

GBM is a very fast-growing type of tumor. In recent years, three of every 100,000 Americans have been diagnosed with GBM, representing the highest incidence rate among malignant brain tumors. Most patients with GBM die of the disease within approximately 14 months of diagnosis.

"These new findings offer critical insights into stratifying patients based on the unique molecular characteristics of their disease," said NCI Director John Niederhuber. "As we learn more and more about the genetic underpinnings of cancer, we hope to achieve a similar level of molecular understanding for all cancers and eventually to generate recipes of highly targeted therapies uniquely suited to the individual patient."

The TCGA researchers expanded on previous studies, which had established gene expression profiling as a means to identify distinct subgroups of GBM.

"We discovered a bundle of events that unequivocally occur almost exclusively within a subtype," said lead author D. Neil Hayes, of University of North Carolina at Chapel Hill. "These are critical events in the history of the tumor's development and spread, and evidence is increasing that they may relate to the initial formation of the tumors."

TCGA researchers reported that the nature of these events indicate that the underlying pathology of each subtype may begin from different types of cells. This may provide a better understanding of which cell types undergo changes that ultimately drive initial cancer formation. This finding has potential clinical significance since determining the types of cells

that form GBM is critical for establishing effective treatment regimens. Because the response to aggressive chemotherapy and radiation differed by subtype, some classes of drugs would be expected to work for some tumor subtypes and not others.

"The ability to differentiate GBM tumors based on their altered genetic code lays the groundwork for more effective treatment strategies to combat this deadly cancer," said NHGRI Director Eric Green. "These findings demonstrate the power of using a cancer's genome to unravel the molecular changes that occur in the various cancer types targeted by TCGA. I'm optimistic that this type of knowledge will someday lead to improved personalized therapies and care for cancer patients."

The new findings build on TCGA's detailed view of GBM genomic changes reported in Nature in October 2008. TCGA was begun in 2006.

TCGA data are being made rapidly available to the research community through a database, http://cancergenome.nih.gov/dataportal.

Obituary:

Lawrence Garfinkel, 88, ACS Epidemiologist

Lawrence Garfinkel, an epidemiologist with the American Cancer Society who led ground-breaking studies establishing links between smoking and other activities with cancer died in Seattle on Jan. 21. He was 88.

The cause was cardiovascular disease, said his son, Martin Garfinkel.

Garfinkel worked for ACS for over 42 years, beginning in 1947 through his retirement in 1989. In the late 1940s, he assisted E. Cuyler Hammond and Daniel Horn in the first ACS prospective mortality study of 187,783 males residing in nine states. Garfinkel coordinated much of the field work of that study, which included training thousands of ACS volunteers in data collection techniques.

When ACS initiated an even larger study in 1959, known as Cancer Prevention Study I (CPS-I), Garfinkel became the co-principal investigator. CPS I enrolled 1 million people in 25 states, and required more than 68,000 ACS volunteers in the data collection effort. During the 1960s, Garfinkel contributed to more than two dozen major papers on the relationship between smoking and health.

Along with colleagues Cuyler Hammond and Oscar Auerbach, Garfinkel coauthored the reported results of some of the first studies that combined epidemiology with pathology. The studies, appearing in the New England Journal of Medicine, provided some of the earliest direct evidence of smoking's damage to the lung, and contributed to the issuance of the landmark Surgeon General's 1964 report on smoking and health.

Garfinkel was born on Jan. 11, 1922, on the Lower East Side of Manhattan, and raised in the South Bronx, to Louis Garfinkel and Sadie Grosshaus, immigrants from Galicia. He attended New York City public schools and served in the Army infantry during World War II. He was seriously wounded in France in August 1944. He graduated from the City College of New York and received his Masters Degree from Columbia University. He was also the recipient of several honorary doctorates.

After Hammond's retirement in 1979, Garfinkel was appointed director of ACS research programs and vice president of epidemiology. Under his guidance, ACS initiated CPS-II which included participants from all 50 states, the District of Columbia, and Puerto Rico. CPS-II remains the largest epidemiological study of its kind ever attempted by medical science. Its contributions were significant and varied. He and his coauthor Steve Stellman, now professor of epidemiology at Columbia University and research director for the World Trade Center Health Registry at the New York City Dept. of Health, published results on female health that was shocking at the time. Their analyses showed that lung cancer mortality rates among smoking females in CPS-II had increased nearly fivefold compared with smoking females in CPS-I, while cancer rates for non-smoking females showed no increase. This information provided convincing evidence that lung cancer was almost exclusively a disease found among smokers.

"He was truly a giant in the field of epidemiology," said Stellman. "He was also kind and modest, and a wonderful collaborator who cared deeply about the volunteers and professional staff that made the ACS a unique research organization."

Garfinkel contributed to well over 100 articles in scientific journals in the fields of epidemiology, cancer, and public health. After his retirement, he continued his work as an ACS volunteer. He also taught biostatistics at the NYU Dental School.

Garfinkel's wife, Celia, died in 1993. He is survived by his brothers Harold, of Margate, Fla., and Melvin, of Farmington, Ct.; son Martin, daughter-in-law Margaret, and two grandchildren, of Seattle; and son Herb, of San Francisco.